
بسم الله الرحمن الرحيم
In The Name Of ALLAH
The Most Gracious, The Most Merciful

Armed Forces College of Medicine

AFCM

Corticosteroids Preparations 1

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture you will be able to:

1)Classify the corticosteroid preparations

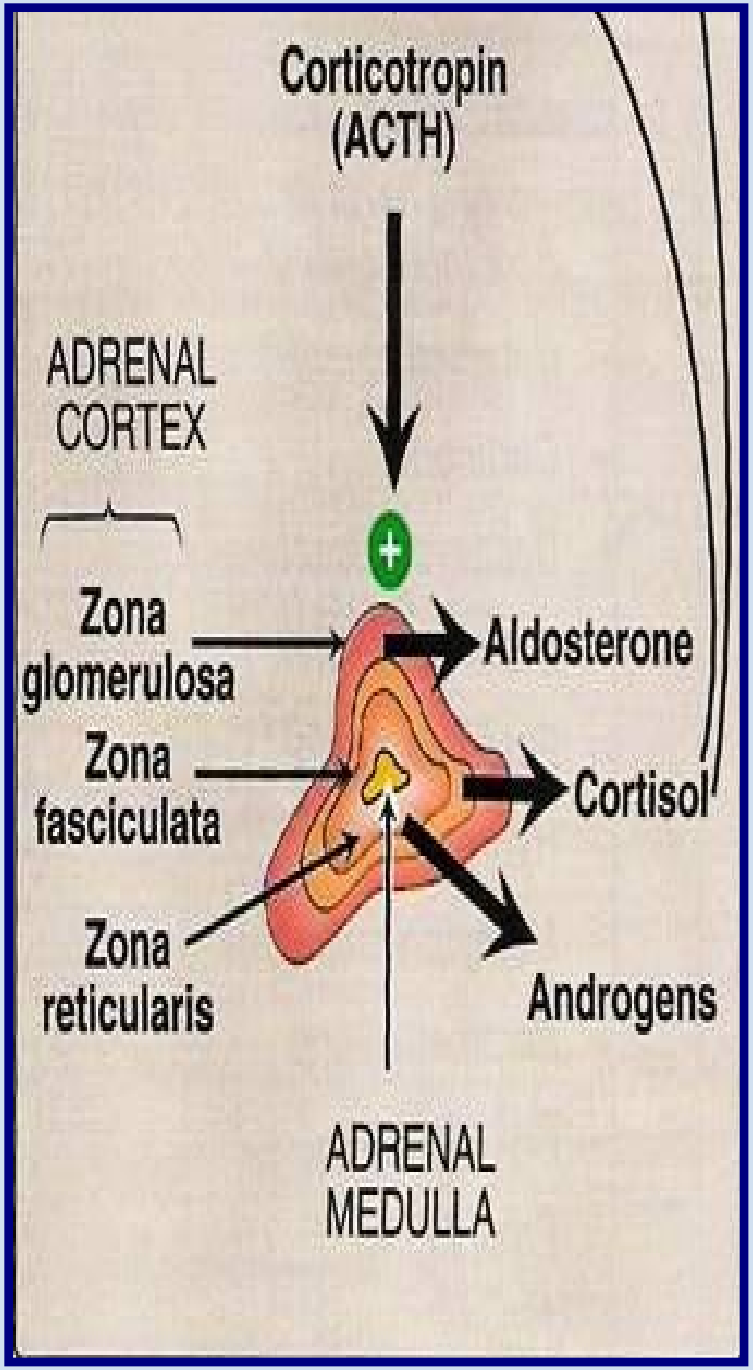
2)Describe the mechanism of action of glucocorticoids

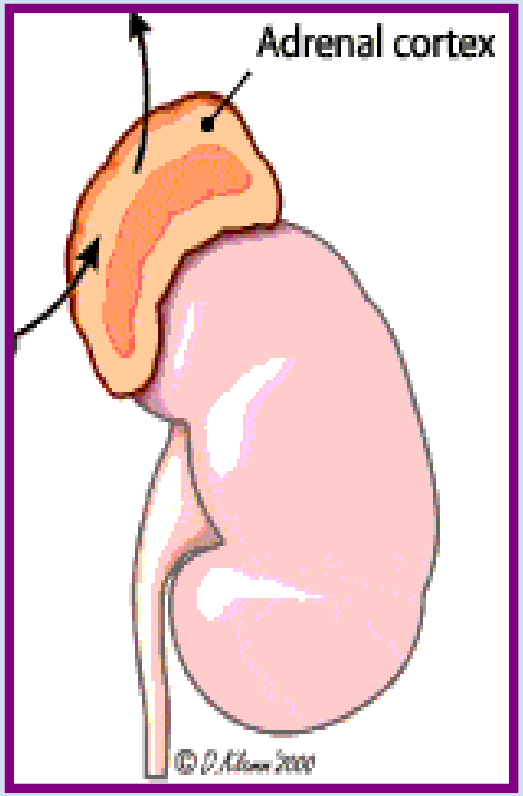
3)Identify the pharmacological actions of glucocorticoids

4)Relate the therapeutic uses of glucocorticoids to their clinical applications

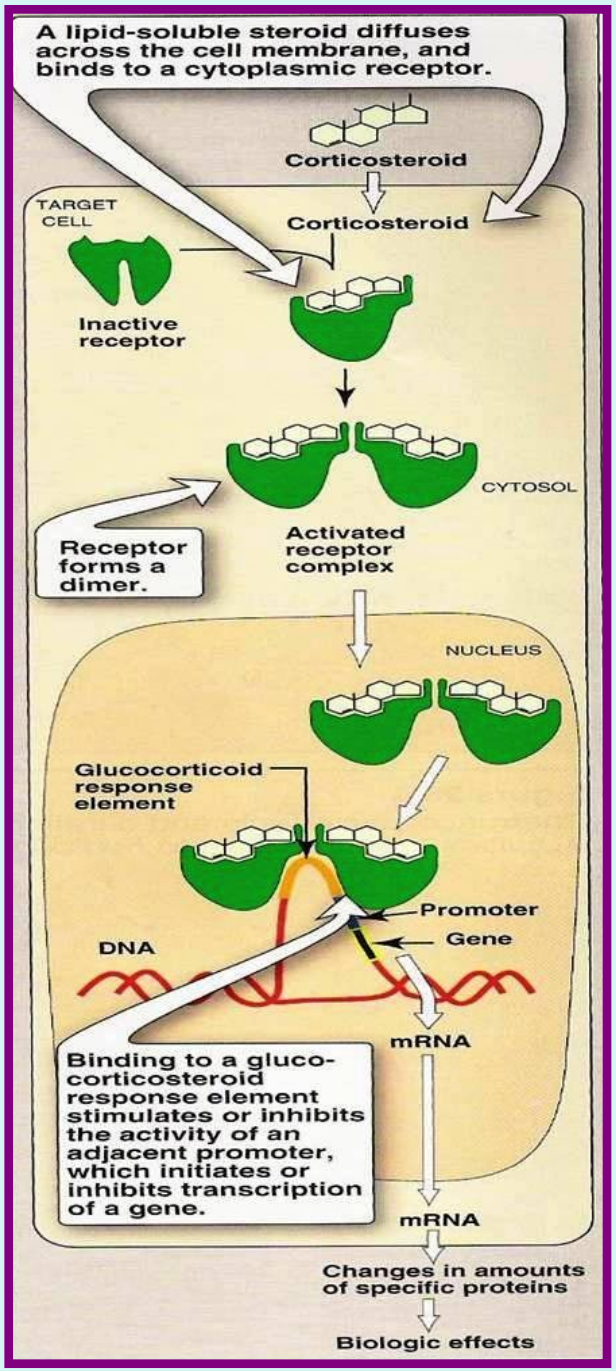
Adrenocortical Hormones

(Corticosteroids)


Corticotropin
(ACTH)
ADRENAL
CORTEX
Zona
glomerulosa
Aldosterone
Zona
fasciculata
Cortisol
Zona
reticularis
Androgens
ADRENAL
MEDULLA


Adrenal cortex

Glucocorticoids



Mechanism of action

- Adrenocorticoids bind to specific intracellular cytoplasmic receptors in target tissues.
- Receptor-Hormone complex translocates into the nucleus.
- R-H complex attaches to gene promoter elements.
- acting as a transcription factor to turn genes on or off, depending on the tissue.
- ***Some Glucocorticoid Effects Are Immediate.***

Pharmacological Actions

(Glucocorticoids)

Hydrocortisone

(Cortisol)

1) Metabolic:

- **Carbohydrate:** **Hyperglycemia**

  → Gluconeogenesis

  → Glycogen synthesis “Glycogenesis” (Liver)

- **Fat** →**Moon face & buffalo hump**

  →Lipolysis → lipemia → Redistribution of fat

- **Protein** → Most tissues →**Catabolic** **(muscle & bone)**

  Delay wound healing → Catabolic effect on fibroblast & C.T

- **Electrolytes** → **mineralocorticoid effect**

  → **Na^+ & water retention** & K^+ depletion

  →**Edema & Hypertension**

2) EU phoria & DEpression

→Psychological disturbances

3) ↓ Pituitary A.C.T.H.

so if **Sudden stop → Addison's Crisis**

4) Cataract & ↑ IOP

5) Gastric ↑ HCl & ↓ mucin →**Peptic ulcer**

6) Blood ..↑ Platelets Coagulation

↓ Lymphocytes

7) Anti – V itamin D →Hypocalcemia

8) **Anti-Inflammatory Effect**

9) Antiallergic effect

10) Immunosuppressive action

Anti-inflammatory Actions:

- Migration of P.M.N.L. to site of inflammation.
- production of prostaglandins and leukotrienes

  [Lipocortin→ phospholipase A2, arachidonic acid]

- Production of inflammatory cytokines (interleukins
- Stabilize the lysosomal membrane & cell death
- Capillary permeability Inflammatory edema

  & joint effusion.

Corticosteroids

Lipocortin

Phospholipid
s

Phospholipase
A2

Arachidonic acids

lipoxygenase

Cycylooxygenase

Leukotriene

Prostaglandins,
Thromboxane
Prostacyclins

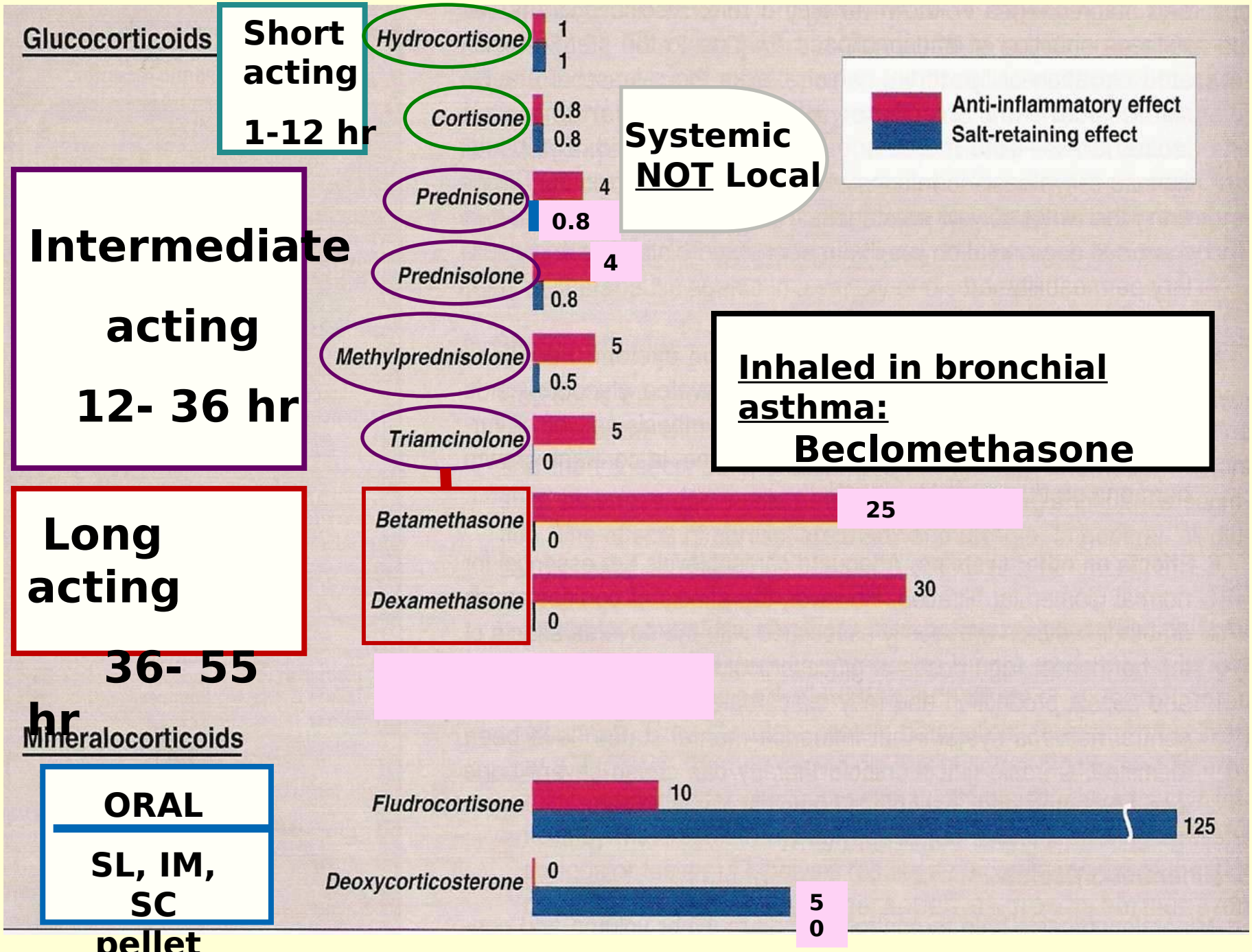
Antiallergic effect:

- ↓antibody formation
- ↓Antigen antibody reaction
- Stabilization of mast cell → ↓ Degratulation → ↓Release of allergic mediators.

∀↓ Tissue response to allergic mediators

Immunosuppressive action:-

- ↓ T-cell proliferation & activation
- ↓ Antibody formation


Glucocorticoids
Short acting
1-12 hr
Hydrocortisone
1
1
Cortisone
0.8
0.8
Systemic
NOT Local
Anti-inflammatory effect
Salt-retaining effect
Prednisone
4
0.8
Intermediate acting
12- 36 hr
Prednisolone
4
0.8
Methylprednisolone
5
0.5
Triamcinolone
5
0
Inhaled in bronchial asthma:
Beclomethasone
Long acting
36- 55 hr
Betamethasone
25
0
Dexamethasone
30
0
Mineralocorticoids
ORAL
SL, IM, SC
pellet
Fludrocortisone
10
125
Deoxycorticosterone
0
5
0

Pharmacokinetics

- Orally are absorbed from the GIT.
- Greater than 90% of the absorbed glucocorticoids are bound to plasma proteins.
- **Prednisone and cortisone** are **prodrugs** activated in liver after absorption into prednisolone and cortisol (hydrocortisone) respectively.
- The ***only*** glucocorticoid that has ***no effect*** on the ***fetus*** in pregnancy is ***prednisone***. It is a ***prodrug*** **that is not converted to the active compound**, *prednisolone, **in the fetal liver***
- Corticosteroids are metabolized by the liver microsomal oxidizing enzymes &Excreted by the kidney.

- when *large doses of the hormone* are required over *an extended period of time* (more than 2 WKs):

  →hypothalamic-pituitary-adrenal (HPA) axis suppression occurs.

- **if HPA suppression occurs:**

  - acute adrenal insufficiency syndrome.

  - psychologic dependence on the drug

  - cause an exacerbation of the disease.

To stop the drug administration:

the dose → tapered & withdrawn gradually

Therapeutic indications

1) Replacement Therapy in Adreno-Cortical Insufficiency

(in Addison's disease**)** → **Use physiological doses**
→ **Almost NO adverse effects:**

Primary Addison's

→ **Replace BOTH** Gluco- & Mineralo-corticoid activities.

Secondary Addison's (↓ ACTH)

→ **Replace ONLY Glucocorticoid activity.**

Replacement Therapy in Addison's disease

a- **Acute Addisonian Crisis**:

- Cortisol I.V. → I.V. infusion / 6 hours
- Saline + Glucose 5% ± Blood transfusion ±Vasopre

b- **Chronic Addison's Disease**:→ Orally

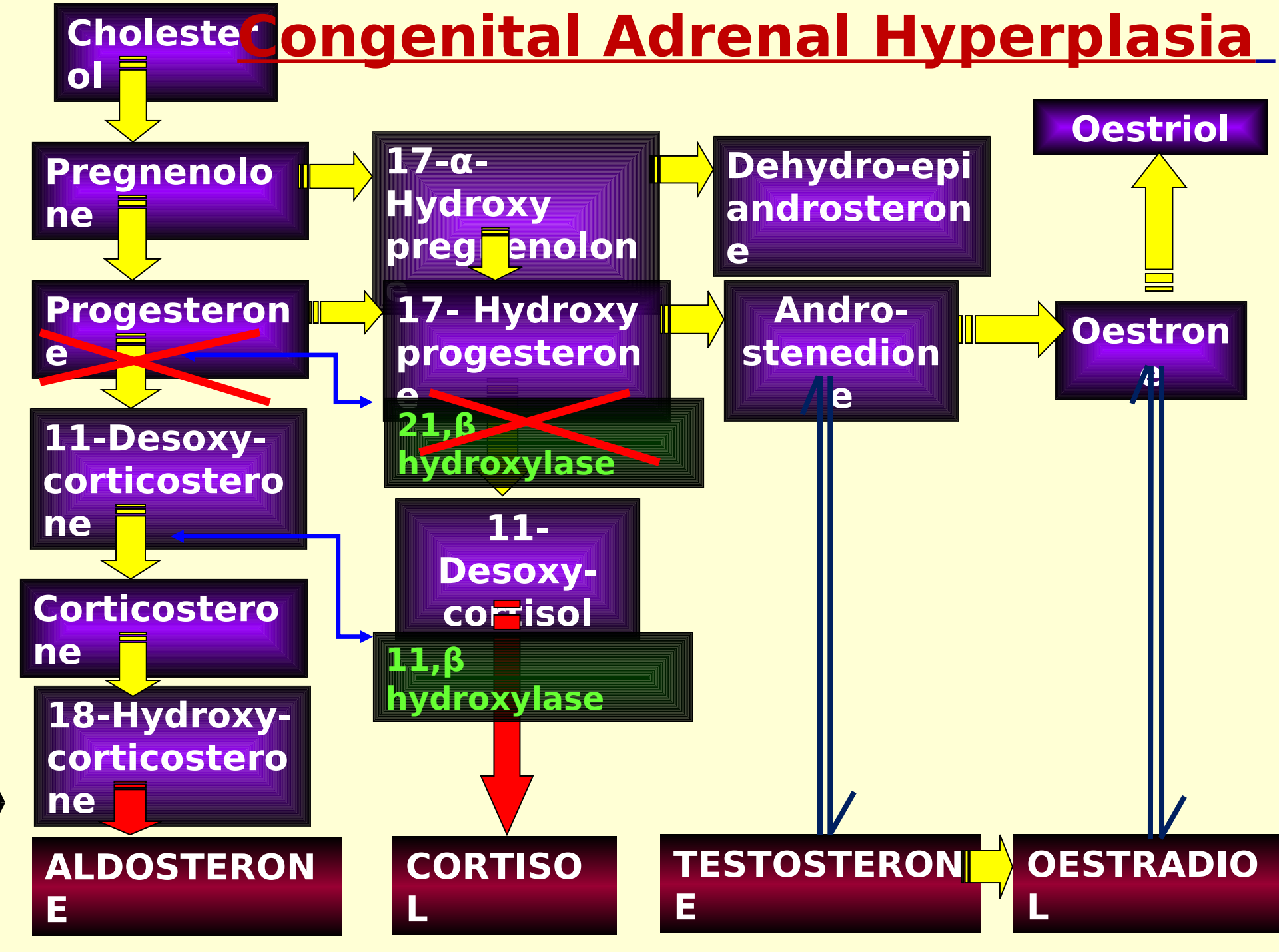
- Gluco.: hydrocortisone (identical to natural cortisone))

+ Generous salt & sugar diet.

- Mineralo.: Fludrocortisone

(minerallocorticoid+ some glucocorticoid activ

Congenital Adrenal Hyperplasia



Congenital Adrenal Hyperplasia

- This condition is also known as **Adrenogenital syndrome**
- **Genetically induced (**autosomal recessive**) enzyme deficiencies** in the pathways that produce steroid hormones leading to a **deficiency of cortisol**. Deficiency of the enzyme **21-hydroxylase accounts for 95%** of affected patients.
- The pituitary secretes massive amounts of the stimulating hormone **corticotropin** to bring the cortisol levels up to normal. This hormone in turn causes the adrenal glands to overproduce certain intermediary hormones which have testosterone-like effects on the fetus and child, leading to so-called **virilization** with accelerated bone maturation and go through puberty very early but ultimately wind up being quite short as adults.
- About **75% of affected infants have the "salt-losing" form** of the disorder, in which the salt-retaining steroid hormone is deficient . This is **potentially fatal if undiagnosed.**
- Treatment involves **hormone replacement.**

2) Anti-inflammatory effect

- reduce the manifestations of inflammations (redness, swelling, heat and tenderness).
- ttt of Active chronic hepatitis,, Acute gout in cases which can not tolerate NSAIDs, Rheumatoid and Osteoarthritic inflammations, and Inflammatory conditions of the skin.

3) Anti-allergic effect

- Used in bronchial asthma, allergic rhinitis, and drug, serum and transfusion allergic reactions

NOT CURATIVE

Beclomethasone dipropionate , triamcinolone are applied topically to the respiratory tract through inhalation from a metered-dose dispenser.

Minimizes Systemic Effects

4) Immunosuppressive

- ***Auto-immune disease:***

  - **Collagen disease**: Polymyositis, polyarthritis & systemic lupus erythematosis.

  - **Blood diseases:** Hemolytic & aplastic anemia, thrombocytopenia & agranulocytosis.

  - **Inflammatory bowel syndrome** e.g. ulcerative colitis.

- ***Suppress organ rejection.***

5) Suppress lymphoid tissues

→ Treat lymphoma & leukemia.

6) Shock & Stress conditions.

Increase glucose level →energy

Corticosteroids are required for normal cardiac function, and their cradiovascular effects are both intropic and vascular (i.e., enhance effects of catecholamines and provide an adrenergic blockade);

Corticosteroids stabilize membranes, enhancing the integrity of capillaries and affecting lysosomal membrane stability

In thyrotoxic crisis it decrease the conversion of T4 to T3 & in graves disease have a suppressive effect on the autoimmune process

Corticosteroids have no immediate effect on anaphylaxis. However, administer them early to try to prevent a potential late-phase reaction (biphasic anaphylaxis).

7) Hypervitaminosis D & Hypercalcemia.

SUGGESTED TEXTBOOKS

1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer

2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.


THANK
YOU